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Special Projects Office (SPO)
Biological Sensors

Good morning, I will be covering the Special Projects Office's efforts in the area of sensors for biological weapon attacks. A comprehensive program for biological warfare defense must provide protection before, during, and after an attack. Biological sensors can contribute to this defense in three distinct ways: forensics, surveillance and early warning.

Forensic testing allows for the identification of the causative agent after public health officials have identified a problem. The technologies currently available fall mostly in the forensics arena.

Alternatively, surveillance sensors must provide an accurate detection and characterization of an attack in time for treatment to be successful. In addition, a surveillance sensor system should provide information that can be used to select the appropriate treatment for exposed personnel; for example, selecting the appropriate antibiotic in the case of an attack with antibiotic resistant strain.

In contrast, early warning sensors do not necessarily need to identify the specific threat, but must be capable of providing a reliable indication of biological threat versus no-threat. Specifically, early warning sensors must provide for a high probability of detection at appropriate sensitivity levels with extremely low levels of false alarm, and they must achieve these goals in a sufficiently short period of time to permit the user to take preemptive action. Ultimately, achieving a very low false alarm rate is the key challenge for early warning sensors, a challenge that becomes increasingly stringent as a defensive network of multiple sensors is proliferated. The Special Projects Office is developing both surveillance and early warning sensor systems.

We find it useful to think of the process of biological agent detection as comprised of five steps. The first step is the collection of the sample. The second step is the sample preparation. The third step is the actual mechanism for the biological identification of the organism. The fourth step is reporting, or transduction of the biological signal to a computer and the final step is analysis. The speed, sensitivity and selectivity in which these steps can be carried out determine the utility of the sensor.

The traditional method of identifying biological organisms, dating back to the late 1800s involves culturing organisms and exploiting various metabolic indicators to differentiate organisms from one another. This type of analysis can take as long as a week, limiting its utility to forensic. More recently, both polymerase chain reaction, or PCR, and antibody-based techniques have been developed for biological agent detection. Traditional approaches for both PCR and antibody detector systems require development of specific PCR primers or specific antibodies for each threat agent, limiting their utility to known and well-studied threats. In addition, both PCR and antibody sensor systems must address challenges in the areas of robust sample preparation protocols and the acceleration of complex reactions to produce a timely result.

The Special Projects Office has three programs for early warning and surveillance sensor systems that attempt to address some of these challenges. The first program, the Biological Time of Flight Mass Spectrotrometer (TOF) is a mass spectrographic device that holds the promise of being sensitive, selective and fast. The second program, TIGER, is a bio-informatic approach that employs a universal PCR primer that can identify all biological agents, both known and unknown agents, including emerging infectious diseases, as well as engineered threats. The third program, the BioAerosol program, is a new effort to develop advanced optical sensors for early warning. This program is just starting up and I look forward to discussing with you ways in which interested groups can become involved. Finally, I will discuss some issues related to the use of sensors for wide area surveillance and ideas about how to address them

The TOF is a fully automated biological sensor system approaching maturity within our office. Brassboards are currently under evaluation and prototypes are nearly complete. The TOF sensor system automatically collects and processes environmental air samples to extract and ionize the collected samples' constituent proteins and small biological molecules. These ionized proteins are weighed using a mass spectrometer.

Then, to determine the biological constituents of the original sample, the observed protein masses can either be compared to specific threat and clutter libraries or to proteomic databases

Within our office, the underlying design philosophy for the TOF has been driven by a signal processing approach, which has attempted to optimize the system design by understanding the impact of each element of the system design on the observed signature to include the signature variability and the competing environmental clutter, not just the signal-to-noise ratio. This approach requires very extensive data collections and system modeling to ensure that we have an adequate understanding of the signature variability and its separability from the competing background clutter. This approach has occasionally produced counter-intuitive results; for example, a requirement for agile laser pointing. However, these requirements are resulting in real and very significant performance improvements. The performance we are observing in the TOF, its speed, sensitivity and selectivity, will make it a strong candidate for a number of important detect-to-warn applications in biological weapons defense. For example, its ability to initiate active defenses in an Immune Building is under investigation. In addition, we are actively engaged in jointly funding elements of the TOF with the Army to ensure its successful transition. We would also welcome discussions with other potential partners who wish to evaluate the TOF performance for their specific applications.

Turning to the second program, under development and evaluation in SPO, the TIGER system is a novel approach for the universal identification of all biological agents, including microbial and viral life. The underlying concept exploits a small set of optimally selected universal PCR primers that capture variable genomic markers. Our hypothesis in TIGER is that these variable markers will provide both hierarchical and species-specific classification. These markers will be compared to a signature library that in most cases will provide species and strain level identification. In cases for which the observed species is not in our library of signatures, the hierarchical TIGER digital signature data will be evaluated to provide a general classification of the unknown sample. Evaluating either environmental or medical samples typically presents to a sensor system a complex mixture—both the TIGER sensor and its companion signal processing algorithms are designed to handle very complex mixtures.

But the real power of TIGER is the ability of the universal primer strategy to always generate a signature, and furthermore a digital signature, even if the sample contains completely novel material.

We are well along the path of verifying and validating the underlying science of TIGER and our hypothesis regarding its operation, and we anticipate that this system will have great potential to serve as the foundation of a future biological surveillance system. We are also conducting active discussions with a number of potential users of TIGER to better understand their requirements for environmental surveillance including medical surveillance and the diagnosis of disease. We hope to establish a number of collaborations in the upcoming year and would look forward to discussing biological surveillance problems with potential users.

The third sensor thrust ongoing in SPO is our new effort focused on developing dramatically improved biological trigger sensors. Current aerosol trigger sensors are based upon optical scattering and fluorescence measurements. Although current sensors offer great utility for many applications, they are plagued by false alarm rates that are higher than desired. Extensive anecdotal data suggest that improved selectivity, and therefore reduced false alarm rates, can be achieved by exploiting alternative optical signatures such as infrared absorption. The new SPO BioAerosol program will selectively exploit the entire electro-magnetic spectrum to determine how to best improve BioAerosol sensor systems. This program will be driven by the same underlying philosophy as the TOF program; namely, it is essential to characterize the signature, the signature variability and the environmental clutter for each specific methodology before a sensor prototype can be designed and built.

We have organized this new program into two distinct tracks. Under the first track, which has already begun, a government team is developing a BioAerosol test-bed as well as a set of detailed protocols for BioAerosol measurements. Under the second track, which will be described in greater detail in a BAA coming out later this year, sensor developers are invited to propose new sensor concepts for advanced BioAerosol triggers. During the first phase, developers must evaluate their sensors concepts with rigorous performance modeling. Developers must validate these models by making measurements at provided BioAerosol

test-bed. Based upon the Phase I modeling and measurements, advanced BioAerosol sensors will be selected for prototype development. We look forward to your interest and participation in this exciting new program.

In addition to these three sensors, our office is interested in the systematic implementation of protective strategies, as evidenced by our ongoing Immune Building Program that was discussed by my colleague Roger Gibbs. In addition to Immune Building, we are exploring strategies for broader bio-surveillance, certain to be a critical element of a future biological weapons defense architecture for both military force protection and homeland defense. One of the critical challenges of a broader architecture, based upon proliferated sensors, is the ever more stringent requirement to reduce individual sensor false alarm rates. To meet this challenge, we are working hard on improved sensors, as you have heard described, and we are beginning to explore distributed sampling architectures that optimize the deployment of samplers and detectors systems based upon a rigorous evaluation of performance.

One example of this approach would be the development of a system for environmental monitoring to determine individual exposure to biological agents, rather than monitoring locations and facilities. Much like personal radiation badges for nuclear workers, a monitor for exposure to biological agents could provide for additional personal protection for critical first responders, while also providing a key element of a surveillance network. These exposure-monitoring devices could be either passive or active devices, and could be either selective or non-selective for particular agents. The preferred embodiment of this device would be small enough to be conveniently worn while performing normal duties. We are interested in ideas for developing this type of personal monitor.

The Special Projects Office is carrying out a coordinated research effort to enable early warning of a biological attack. Please feel free to contact me with new approaches to achieving this goal.